UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/824,134	04/03/2001	David Wallach	WALLACH=16A	2547

1444 7590 11/21/2006

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
DAVIS, MINH TAM B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 11/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/824,134
Filing Date: April 03, 2001
Appellant(s): WALLACH ET AL.

ROGER L. BROWDY
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 19, 2006 appealing from the Office action mailed June 06, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Burgess et al. "Possible dissociation of the heparin-binding and mitogenic activities of heparin-binding (acidic fibroblast) growth factor-1 from its receptor-binding activities by site-

directed mutagenesis of a single lysine residue". Journal of Cell Biology, vol. 11 (November 1990), pp. 2129-2138.

Gillies et al. "Antigen binding and biological activities of engineered mutant chimeric antibodies with human specificities". Human Antibodies and Hybridomas, vol.1, no.1 (1990), pp.47-54.

Lazar et al. "Transforming growth factor alpha: Mutation of Aspartic acid 47 and Leucine 48 results in different biological activities". Molecular and Cell Biology, vol. 8, no.3 (Mar. 1988), pp. 1247-1252.

Renate et al. "Secondary structure of the third extracellular loop responsible for ligand selectivity of a mammalian gonadotropin-releasing hormone receptor". Journal of Medicinal Chemistry (United States), vol. 45, no. 5 (2002): pp. 1026-1034.

Tao et al. "Studies of aglycosylated chimeric mouse-human IgG. Role of carbohydrate in the structure and effector functions mediated by the human IgG constant region". The Journal of Immunology, vol.143, no.8 (October 15, 1989), pp. 2595-2601.

Wilson et al. "The structure, organization, activation and plasticity of the erythropoietin receptor". Current Opinion in Structural biology, vol. 9, no.6, (1999), pp.696-704

Yoshikawa et al. "The distinct agonistic properties of the phenypyrazolosteroid cortivazol reveal interdomain communication within the glucocorticoid receptor". Molecular Endocrinology, vol.19, no.5 (2005), pp. 1110-1124.

Zhang et al. "Estrogen stimulates release of secreted amyloid precursor protein from primary rat cortical neuron via protein kinase C pathway". Acta Pharmacoligica Sinica, vol. 26, no.2 (February 2005), pp. 171-176.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7, 11, 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-7, 11, 14 are indefinite, because claims 1-2 recite "moderately stringent hybridization conditions". Moderately stringent conditions are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree of moderately stringent conditions and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention and would not be able to determine the metes and bounds of the claims.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 11, 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is dawn to an isolated DNA molecule comprising:

1) a DNA sequence which encodes the MORT-1 protein, having the amino acid sequence of SEQ ID NO:2;

2) a DNA sequence that encodes an analog of MORT-1 protein of SEQ ID NO:2, which analog binds with the intracellular domain of the FAS ligand receptor (FAS-IC), which DNA sequence is capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions; or

3) a DNA coding sequence consisting of a DNA sequence which encodes a fragment of said MORT-1 protein which binds with FAS-IC.

Claim 2 is drawn to an isolated DNA molecule of claim 1, comprising a DNA sequence that encodes an analog of said MORT-1 protein of SEQ ID NO:2, which binds with the intracellular domain of the FAS ligand receptor (FAS-IC), which DNA sequence is capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions.

Claims 3-7 are drawn to a vector comprising a DNA sequence according to claim 1 (claim 3), which is capable of being expressed in a eukaryotic host cell (claim 4), or in a prokaryotic host cell (claim 5), an isolated transformed eukaryotic or prokaryotic host cell containing a vector of claim 3 (claim 6), and a method producing a polypeptide which binds with the intracellular domain of the FAS ligand receptor (claim 7).

Claim 11 is drawn to a recombinant animal virus vector encoding a viral surface protein capable of binding a specific target cell surface receptor, and further including the sequence of a DNA molecule of claim 1.

Claim 14 is drawn to an isolated DNA molecule of claim 1, wherein the entire said DNA sequence is a coding sequence encoding said polypeptide.

The specification discloses isolation of the claimed polynucleotide sequence, which encodes a MORT-1 protein or SEQ ID NO:2. The specification discloses that transfection of cells with HF-1, which is the same as the claimed polynucleotide sequence, which encodes a MORT-1 protein or SEQ ID NO:2, as well as p55-IC and FAS-IC, results in significant cell death, greater than that caused by FAS-IC expression (page 42, 4th paragraph, and figure 6). The specification however also discloses that high expression of p55-IC alone triggers a cytocidal effect, and that the expression of Fas-IC alone in Hela cells also have such an effect, although to a lower extent (page 42, 4th paragraph). Thus, it is not clear whether cell death is due to the activation of FAS ligand receptor by MORT-1 protein or due to the expression of p55-IC in the above transfected cells. The specification discloses that MORT-1 protein encoded by the claimed DNA sequence is also capable of activating cell cytoxicity on its own (p. 7, last paragraph). The specification however does not disclose which domain of the MORT-1 protein or SEQ ID NO:2 is responsible for activating cytotoxicity.

The specification further discloses that only via it's own "death domain" comprising the amino acid sequence of residues 153 to 215 of SEQ ID NO:2, MORT-1 can bind to the FAS ligand receptor, via the "death domain" of the FAS ligand receptor, which is located within the intracellular domain of the FAS ligand receptor (page 36 and table 1 on page 37). The

specification discloses that co-expression of the C-terminal amino acids 130-245 of MORT-1 protein, which contains the MORT-1 death domain homology region and FAS ligand receptor (FAS-R) strongly interferes with FAS induced (i.e. FAS-R mediated) cell death, as would be expected from the ability of the MORT-1 death domain homology region to bind to the FAS-R death domain (p.44, last three paragraph, p.45, and figure 7). In figure 7, the C-terminal consisting of amino acids 130-245 of SEQ ID NO:2 that binds to the intracellular domain of the FAS ligand receptor (FAS-IC) acts as an antagonist, and interferes with the binding of an antibody specific for FAS receptor (FAS-R), which antibody is capable of inducing apoptosis, and consequently inhibiting FAS-R mediated cytotoxicity.The specification discloses that the N-terminal part of MORT-1 does not interfere with FAS-R mediated cell death, and if at all, slightly increases cell death.

Due to the indefinite language of " hybridization under moderately stringent conditions", which is a relative term, supra, a DNA sequence hybridizing under moderately stringent conditions with the DNA sequence encoding SEQ ID NO:2 encodes a peptide or protein of any size, and unknown structure, wherein said peptide or protein does not have to share a substantial sequence homology with SEQ ID NO:2. The encoded variants of SEQ ID NO:2 could have deletion, or substitution or insertion, throughout the sequence at any amino acid position, provided that they binds to FAS-IC. In other words, a DNA sequence, that has the ability to hybridize to the cDNA encoding SEQ ID NO:2 under the "undefined moderately stringent conditions", does not define the structure of "a DNA sequence encoding a sequence that binds to FAS-IC".

The claims, as written, encompass a genus of DNA sequences of any size, which encodes unknown amino acid sequences of any size, and unknown structure, wherein said sequences bind with any affinity to any region of FAS-IC and not necessarily to the FAS death domain within the FAS-IC, and wherein said DNA sequences do not have to share a substantial sequence homology with the DNA sequence encoding SEQ ID NO:2. The encoded variants of SEQ ID NO:2 could have substitutions or deletions or insertions, provided that they bind to FAS-IC. In other words, the genus of encoded analogs **encompass a genus of peptide or protein ligands of unknown structure, that bind to FAS-IC with any affinity, ranging from very low affinity to very high affinity, such as peptide mimetic, agonist, or antagonist**, wherein the structure of said ligands does not have to be substantially similar to that of SEQ ID NO:2, or its C-terminal amino acids 130-245.

The specification however does not describe structure of any of the claimed DNA sequences encoding a genus of analogs, other than the DNA sequence encoding SEQ ID NO:2, and its fragments consisting of the "death domain" consisting the amino acid sequence of residues 153 to 215 of SEQ ID NO:2, and the C-terminal amino acids 130-245 of SEQ ID NO:2.

It is noted that binding to FAS-IC by itself is not a definitive function, such function defines MORT-1, such as the agonist function of inducing cytotoxicity or the antagonist function of inhibiting FAS-induced cytotoxicity, because binding to FAS-IC alone is not sufficient for the property of activation of FAS ligand receptor or the property of displacing the binding of FAS ligand to its receptor for the following reasons. It is well known in the art that although there is certain plasticity in ligand-receptor interactions, a ligand has to have a certain binding affinity or stability, and has to have molecular configuration specificity, for example, a certain

configuration for perfect fit into the receptor for activation of the receptor, like lock and key . For example, Zhang et al, 2005, Acta Pharmacoligica Sinica, 26(2): 171-176 teach that the effect of an estrogen ligand requires molecular configuration specificity of the ligand. Yoshikawa Noritada et al, 2005, Molecular endocrinology, 19 (5):p1110-24, teach that for activation of the glucocorticoid receptor, stable conformational changes of the ligand binding domain, induced by binding of the receptor to the ligand seem to be necessary for activation of the receptor. Wilson I A et al, 1999, Current opinion in structural biology (ENGLAND), 9 (6): p696-704, teach that erythropoietin receptor activation is dependent on the actual configuration of the receptor-ligand dimer assembly. Petry Renate et al, 2002, Journal of medicinal chemistry (United States), 45 (5): p1026-34, teach that stabilization of a particular structural state of the receptor, and further induction of conformational rearrangements of the receptor by the ligand is necessary for receptor activation. In view of the art, one cannot predict that the claimed analog would activate the FAS receptor or act as an antagonist and displacing the binding of the FAS ligand. For example, one cannot predict whether the claimed analog would have the molecular configuration specificity required for FAS receptor activation, or would stabilize a certain particular structural state of the FAS receptor or would induce certain conformational changes of the FAS receptor, that might be required for FAS receptor activation.

Further, although there is a correlation between structure of the C-terminal amino acids 130-245 of SEQ ID NO:2 and the function of inhibiting FAS induced cytotoxicity, there is **no correlation between structure and the property of binding to FAS-IC**, because there is no disclosed common structure between compounds that bind to FAS-IC, such as antibodies to

FAS-IC, or FAS ligand, that also bind to FAS-IC, and SEQ ID NO:2 or its amino acids 153-215, or 130-245.

Thus, not only binding to FAS-IC is not a definitive function, there is **not even a correlation between structure and the function of binding to FAS-IC**, because there is no correlation between structure and the property of binding to FAS-IC, supra, and because a DNA sequence, that has the ability to hybridize to the cDNA encoding SEQ ID NO:2 under "undefined moderately stringent conditions", does not define the structure of "a DNA sequence encoding a sequence that binds to FAS-IC", supra. In view of the above, there is no correlation between structure and the genus of analogs.

Further, **the disclosed single DNA sequence encoding SEQ ID NO:2, or its amino acids 153-215, or 130-245 of SEQ ID NO:2 is not representative species**, because the encompassed encoded analogs are of unknown structure and because there is no disclosed common structure feature between the encompassed genus of analogs and SEQ ID NO:2, or its amino acids 153-215, or130-245, which feature constitutes a substantial portion of the genus.

The instant disclosure of a single species of nucleic acid does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length genes. A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional

features of the claimed genus of polynucleotides. There is no description of the conserved regions, which are critical to the structure and function of the genus claimed. There is no description, however, regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, no identifying characteristic or property of the instant genus of polynucleotides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the DNA sequences encoding a genus of analogs, and because the genus is highly variant, the disclosure of specific nucleotide sequences, the DNA sequence encoding SEQ ID NO:2 or its C-terminal amino acids 130-245 of SEQ ID NO:2 and the ability to screen, is insufficient to describe the DNA sequences encoding a genus of analogs. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the DNA sequence encoding a genus of analogs as broadly claimed. Thus, the claims and the specification do not meet the written description provisions of 35 USC 112, first paragraph, and one would conclude that Appellant did not have possession of the claimed DNA sequences encoding a genus of analogs at the time the invention was made.

Claim Rejections - 35 USC § 112, First Paragraph, Scope

Claims 1-7, 11, 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA sequence encoding SEQ ID NO:2, or a fragment thereof comprising amino acids 130-245 of SEQ ID NO:2, does not reasonably provide

enablement for 1) a DNA sequence encoding an analog of SEQ ID NO:2, which analog binds with the intracellular domain of the FAS ligand receptor (FAS-IC), which DNA sequence is capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions, or 2) a DNA coding sequence consisting of a DNA sequence which encodes a fragment of said MORT-1 protein which binds with FAS-IC. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claim 1 is dawn to an isolated DNA molecule comprising:

1) a DNA sequence which encodes the MORT-1 protein, having the amino acid sequence of SEQ ID NO:2;

2) a DNA sequence that encodes an analog of MORT-1 protein of SEQ ID NO:2, which analog binds with the intracellular domain of the FAS ligand receptor (FAS-IC), which DNA sequence is capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions; or

3) a DNA coding sequence consisting of a DNA sequence which encodes a fragment of said MORT-1 protein which binds with FAS-IC.

Claim 2 is drawn to an isolated DNA molecule of claim 1, comprising a DNA sequence that encodes an analog of said MORT-1 protein of SEQ ID NO:2, which binds with the intracellular domain of the FAS ligand receptor (FAS-IC), which DNA sequence is capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions.

Claims 3-7 are drawn to a vector comprising a DNA sequence according to claim 1 (claim 3), which is capable of being expressed in a eukaryotic host cell (claim 4), or in a

prokaryotic host cell (claim 5), an isolated transformed eukaryotic or prokaryotic host cell containing a vector of claim 3 (claim 6), and a method producing a polypeptide which binds with the intracellular domain of the FAS ligand receptor (claim 7).

Claim 11 is drawn to a recombinant animal virus vector encoding a viral surface protein capable of binding a specific target cell surface receptor, and further including the sequence of a DNA molecule of claim 1.

Claim 14 is drawn to an isolated DNA molecule of claim 1, wherein the entire said DNA sequence is a coding sequence encoding said polypeptide.

The claimed DNA sequences encode a genus of analogs, which encompass a genus of peptide or protein ligands of unknown structure, that bind to FAS-IC with any binding affinity, ranging from very low affinity to very high binding affinity, such as peptide mimetics, any agonist, or antagonist, wherein the structure said ligands do not have to be substantially similar to that of SEQ ID NO:2, or its C-terminal amino acids 130-245.

The disclosure of the specification has been set forth above.

One cannot extrapolate the teaching in the specification to the claims, because one cannot predict which of the encoded analogs, or the encoded fragments of SEQ ID NO:2 that bind with FAS-IC, would have the property of SEQ ID NO:2, such as activation of cytotoxicity, or the property of the C-terminal amino acids 130-245 of SEQ ID NO:2, such as inhibition of FAS-induced cytotoxicity, to have any practical, real world use. It is noted that protein chemistry is probably one of the most unpredictable areas of biotechnology, and such unpredictability would equally apply to DNA sequences which encode proteins. For example, replacement of a single lysine residue at position 118 of acidic fibroblast growth factor by glutamic acid led to the

substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al. Journal of Cell Biology, 1990, 11: 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cell Biology, 1988, 8: 1247-1252). Similarly, it has been shown that aglycosylation of antibodies reduces the resistance of the antibodies to proteolytic degradation, while CH2 deletions increase the binding affinity of the antibodies (see Tao. et al, 1989, The Journal of Immunology, 143(8): 2595-2601, and Gillies et al, 1990, Human Antibodies and Hybridomas, 1990, 1(1): 47-54). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. In view of the above unpredictability of protein chermistry , and further in view that binding to FAS-IC by itself is not sufficient for the activation of FAS ligand receptor or displacing the binding of FAS ligand to its receptor, supra, one cannot predict that which of the claimed analogs or fragments of SEQ ID NO:2 that bind to FAS-IC would have the property or function of SEQ ID NO:2, or the C-terminal amino acids 130-245 of SEQ ID NO:2 to have any practical, real world use.

Further, the claims encompass polynucleotides comprising non-disclosed nucleic acid sequences attached to a polynucleotide that encode a peptide fragment that binds to FAS-IC; that is polynucleotides that hybridize to said polynucleotides under the undefined moderately stringent conditions . When given the broadest reasonable interpretation, it would be expected that a substantial number of the hybridizing molecules encompassed by the claims **would not**

share either structural or functional properties with the polynucleotide that encode MORT-1 protein of SEQ ID NO:2.

In view of the above, one would not know how to make the claimed DNA sequences encoding analogs or fragments of SEQ ID NO:2 that bind to FAS-IC, such that they would be of any practical use, such as activation of cytotoxicity or inhibition of FAS-induced cytotoxicity.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature ot the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

Given the unpredictability of protein chemistry, which applies as well to DNA sequences encoding proteins, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

(10) Response to Argument

Piecemeal Prosecution

Appellant argues that prosecution was piecemeal because the 112 second paragraph rejection, and 112, first paragraph, written description, and scope of enablement rejections were reinstated in the Office action of June 06, 2005.

The Examiner apologizes for any inconvenience due to the reinstation of the 112, second and first paragraph rejections. The Examiner takes note however that the issues remain the same, regardless that the rejection was withdrawn and then reinstated after further review and reconsideration.

Claim Rejections - 35 USC § 112, Second Paragraph

Claims 1-7, 11, 14 remain rejected under 35 USC 112, Second Paragraph, for the use of the indefinite language "moderately stringent conditions" in claims 1-2.

Appellant argues that US 5,026,636 defines moderate stringency as conditions that allow detection of sequences at least 75% homologous to the probe and that the conditions could be readily determined using a reference text for guidance. Applicant argues that US 4,968,607, US 5,198,342, US 5,262,522, and US 5,237,051, all have claims that include the term "moderate stringency". Appellant recites Ausubel et al, 1987-1998, Current protocols in Molecular Biol, which teaches how to determine moderate stringency wash conditions, by calculating the decrease in temperature required using the correlation for decrease in Tm percent mismatch. Appellant argues that not only because the use of such term by many different inventors, and allowed by many different examiners is evidence that the terminology is considered sufficiently

definite by the art, but also reinterpretation of the definiteness of such claims by the PTO casts a shadow of doubt on previously issued "moderately stringency" claims. Appellant suggests that the term "hybridization under moderately stringent conditions" is interpreted as those conditions that permit detection of nucleotide sequences at least approximately 75% homologous. Appellant argues that thus, based on the teaching in the art, the scope of "moderate stringency" could be determined.

Appellant argues that the Examiner has not cited any reference to show that one of ordinary skill in the art would consider the term to be other than what Appellant have established. Concerning the fact that moderate is a relative term, Appellant recites MPEP 2173.05(b) stating that the claim language, including terms of degree, may not be precise, does not automatically render the claim indefinite under 112, second paragraph, and that acceptability of the language depends on whether one of ordinary skill in the art would understand what is claimed, in light of the specification. Appellant argues that there is no rejection over the prior art.

The arguments are not found to be persuasive.

MPEP 2173.05(b) teaches that "While, as a general proposition, broadening modifiers are standard tools in claim drafting in order to avoid reliance on the doctrine of equivalents in infringement actions, when the scope of the claim is unclear a rejection under 35 U.S.C. 112, second paragraph, is proper. See In re Wiggins, 488 F. 2d 538, 541, 179 USPQ 421, 423 (CCPA 1973)". Further, it is noted that as cited by Appellant, MPEP 2173.05(b) teaches that **acceptability of a relative term depends** on whether one of ordinary skill in the art would understand what is claimed, **in light of the specification** (emphasis added). Since there is no definition of moderately stringent hybridization conditions in the instant specification, and since

"moderate" is a relative term, one of ordinary skill in the art cannot determine the metes and bound of the claimed invention. For the instant application, the specification does not provide a standard for ascertaining the requisite degree, therefore, one of ordinary skill in the art would not be reasonably apprised of the scope of the claimed hybridization conditions. A claim is indefinite where those skilled in the art would not understand what is claimed, when reading the claim language in light of the specification. *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1218, 18 USPQ2d 1016, 1030 (Fed. Cir. 1991); *Texas Instruments Inc. v. United States Intl Trade Common*, 871 F.2d 1054, 1063, 10 USPQ2d 1257, 1263-64 (Fed. Cir. 1989); *Orthokinetics, Inc.*, 806 F.2d at 1576, 1 USPQ2d at 1088.

Further, although some US patents use the "moderately stringent hybridization conditions" language in the claims, or define the language, it is noted that that each cases is determined on its own and that "**acceptability of the language** depends on whether one of ordinary skill in the art would understand what is claimed, **in light of the specification**" (emphasis added) (MPEP 2173.05(b)). Appellant has not shown that the disclosure of the instant specification is similar to the specifications of those patents that have the instantly claimed language in their claims. The Examiner takes note that the particular definition by another US patent, or the specific moderate stringency wash taught by Ausebel et al would be just one of possible numerous reasonable interpretations of the instantly claimed moderately stringent hybridization conditions, in view of the lack of definition of the term in the instant application, and in view that the instant specification does not provide a standard for ascertaining the requisite degree and further in view that moderate is a relative term, and one cannot determine the metes and bound of the claimed invention, supra. In addition, no rejection over the prior art is

not an issue here. The issue here is that one of ordinary skill in the art cannot determine the scope of the claims, and that the metes and bound of the claims cannot be determined.

Appellant again argues that the rejection was withdrawn in earlier Office actions, and thus the reinsertion of the rejection by the same Examiner should be given very little weight.

The Examiner apologizes for any inconvenience made. However, the issue remains the same, regardless that the rejection was withdrawn, and then reinstated after further review and reconsideration.

Claim Rejections - 35 USC § 112, First Paragraph, Written Description

Claims 1-7, 11, 14 remain rejected under 35 USC 112, first paragraph, for lack of a clear written description of the analogs encoded by the claimed DNA sequence.

A. Appellant argues that the claimed analog is defined by a complete or partial structure or other physical and/or chemical properties. Appellant argues that the Examiner concedes that binding is a physical property. Appellant argues that there is effectively a partial structure because the DNA encoding it must be capable of hybridizing to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions. Appellant argues that this combination of partial structure and physical/and or chemical properties is sufficient to show that Appellant was in possession of the claimed invention.

The arguments are not found to be persuasive.

Contrary to Appellant's arguments, the claimed DNA sequence encoding a genus of analog is not defined by a complete or partial structure or critical function and/or other chemical properties. The claimed DNA sequence, that has the ability to hybridize to the cDNA encoding

SEQ ID NO:2 under "moderately stringent conditions", does not define the structure of "a DNA sequence encoding a sequence that binds to FAS-IC", because, due to the indefinite language "hybridization under moderately stringent conditions", the hybridizing species not only could be of any size, but also does not have to have a substantial similarity with the DNA sequence encoding SEQ ID NO:2 or its amino acids 130-245, e.g. having substitutions, or deletions or insertions, at any position, provided that the encoded peptide or protein binds to FAS-IC, even with extremely low binding affinity.

The specification however does not teach the structure of any of the claimed DNA sequences encoding a genus of analogs, other than the DNA sequence encoding SEQ ID NO:2 and its amino acids 153-215 or 130-245 of SEQ ID NO:2. The specification does not disclose **which nucleotides could be deleted or substituted or inserted, such that the encoded analog still could bind to FAS-IC**, a preliminary requirement before inducing cytotoxicity or inhibiting FAS-induced cytotoxicity, or could bind to FAS-IC with sufficient affinity to confer any useful, critical function.

Further, it is noted that although binding to FAS-IC by itself is a physical property, such physical property is not a definitive physical property that defines the claimed invention, and distinguishes the claimed invention from others, because there are also are other proteins such as anti-FAS-IC antibodies or FAS ligands that also bind to FAS-IC, but would have a different physical and chemical properties than the claimed analogs, and because Appellant has not shown that binding alone confers a physical property necessary for the critical function of the claimed sequences, such critical function defines the claimed invention from others, e.g., inducing cytotoxicity or inhibiting FAS-induced cytotoxicity.

Thus one would conclude that claimed DNA sequence encoding a genus of analog is not defined by a complete or partial structure or other critical physical and/or chemical properties. It is noted that At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention" In *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412).

B. In a new argument, Appellant asserts that binding alone is sufficient to establish the function of serving in affinity chromatograph to isolate FAS-IC protein, or to characterize additional proteins, factors, receptors etc.. which are capable of binding to the MORT-1 protein.

The arguments are not found to be persuasive.

Binding to FAS-IC by itself is not a definitive function, such function defines and distinguishes the claimed invention from others, such as inducing cytotoxicity or inhibiting FAS-induced cytotoxicity, because binding to FAS-IC alone is not sufficient for the activation of FAS ligand receptor or displacing the binding of FAS ligand to its receptor, supra.

Moreover, concerning Appellant's new arguments that binding alone is sufficient to establish the function of serving the affinity chromatograph to isolate proteins or factor or receptors that bind to MORT-1 protein, such as FAS-IC protein, it is noted that the encompassed genus of analogs could bind to FAS-IC with **any** affinity, for example, with extremely low affinity, and thus the proteins, that bind to the affinity column made of the claimed analogs, do not necessarily have any effect or correlation with SEQ ID NO:2 (MORT-1), or FAS-IC protein.

The specification however **does not disclose which structure of the claimed genus of analogs has sufficient affinity,** such that they could be used for affinity chromatograph to

isolate FAS-IC or FAS receptor, other than SEQ ID NO:2 and its amino acids 153-215 or 130-245 of SEQ ID NO:2.

It is noted that disclosure of a method to screen for analogs that bind to FAS-IC does not meet the 112, first paragraph, written description requirement. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

Further, it is noted that in a recent 2004 court case (*Rochester v. Searle*, 358 F.3d 916, Fed Cir., 2004), the court states that "even with the three dimensional of enzymes such as COX-1 and COX-2 in hand, it may even now not be within the ordinary skill in the art to predict what compounds might bind to and inhibit them". The present application is similar to that in *Rochester* case, in that although the structure of some FAS-IC and FAS receptor is known in the art, and except for SEQ ID NO:2, and its amino acids 153-215 or 130-245, one cannot predict what mimetics or which peptide or polypeptide might bind to FAS-IC, or might bind to FAS-IC with sufficient affinity, so that they can be used for affinity column, or as an agonist or an antagonist, especially in view that three dimensional structure of FAS-IC or FAS receptor is not even disclosed in the specification or known in the art.

C. Concerning the issue of only a single disclosed species, Appellant asserts that similar to Example 14, the instant specification exemplifies a MORT protein that binds to FAS-IC, and contemplates analogs of the protein, wherein the variants is encoded by a DNA molecule that hybridizes to the MORT-1 encoding DNA molecule under moderately stringent conditions.

Appellant argues that the instant specification indicates that procedure for making such analogs, including modification of the DNA sequence encoding them are routine in the art, and provides an assay for determining whether a given protein binds to FAS-IC. Appellant argues that thus the single species disclosed is representative of the genus and an assay is present for identifying the members of variants that are capable of the specified functionality.

The arguments are not found to be persuasive.

The instant description of the claimed analogs is not commensurate with Example 14. In Example 14, the variant has substantial similarity with SEQ ID NO:3, i.e. having at least the same length or longer than SEQ ID NO:3, and 95% sequence similarity with SEQ ID NO:3, and also has the critical function of the well known catalytic reaction of SEQ ID NO:3. On the contrary, the encoded analog of the instant application does not have to have substantial similarity with SEQ ID NO:2 or its fragment consisting of the C-terminal amino acids 130-245 of SEQ ID NO:2, due to the indefinite language "moderately hydridization conditions", supra. The encompassed genus of analogs could be of any size, such as **small peptide mimetic, agonist or antagonist, with unknown structure**, provided that they bind to FAS-IC, and that the encoding DNA sequence thereof hybridizes to the DNA sequence encoding SEQ ID NO:2 under "undefined moderately" stringent conditions. Further, different from Example 14, wherein the variant has the same critical function of SEQ ID NO:3, in the instant application, not only the encoded analog does not have to be substantially similar to the full length DNA sequence encoding SEQ ID NO:2, the analog does not have the critical or definitive function of SEQ ID NO:2, such function defines the claimed invention, and distinguishes the claimed invention from others, such as inducing cytotoxicity, or inhibiting the FAS-induced cytotoxicity, because

binding to FAS-IC per se is not sufficient for the activation of FAS ligand receptor or displacing the binding of FAS ligand to its receptor, supra.

In addition, in the instant application, there is no disclosed common structure between the genus of encoded analogs, and SEQ ID NO:2, or residues 153 to 215 of SEQ ID NO:2, or the C-terminal amino acids 130-245 of SEQ ID NO:2, which common structure constitutes a portion of the genus, and is necessary to define the genus.

Thus, in view of the above, contrary to Appellant's arguments, the disclosed single DNA sequence encoding MORT-1 protein SEQ ID NO:2, and its amino acids 153-215, and 130-245 are not a representative species of the claimed DNA sequences encoding a genus of analog.

D. Appellant argues that the hybridization language is acceptable, reciting Example 9. Appellant argues that based on the analysis of Example 9, the claimed invention is adequately described.

The arguments are not found to be persuasive.

The instant description of the claimed analogs is not commensurate with Example 9. In Example 9, the highly stringent conditions are defined in the specification, i.e. 6xSCC at 65^0 C. On the contrary the instant "moderately stringent conditions" are not defined in the instant specification, and therefore, one cannot determine the scope of the "moderately stringent hybridization conditions", supra. Further, in Example 9, the encoded protein also has the critical function of not only binding to a dopamine receptor but also stimulating adenylate cyclase activity . On the contrary, the instant encoded analog only binds to FAS-IC, wherein binding to

FAS-IC per se is not sufficient to induce cytotoxicity or inhibit FAS-induced cytotoxicity, the critical function of the encoded SEQ ID NO:2, or its C-terminal amino acids 130-245, supra.

E. Appellant argues that binding alone is an important function as it allows FAS-IC to be isolated by affinity chromatography, and that it is definitive as it is easy to determine whether any given analog of MORT-1 has such binding capability.

The arguments are not found to be persuasive.

Binding to FAS-IC per se is not sufficient for making affinity chromatography to isolate proteins that bind to SEQ ID NO:2, because not any sequence that binds to FAS-IC would have sufficient affinity for use in affinity column to isolate FAS-IC or FAS receptor, supra. The specification however does not describe which analogs that bind to FAS-IC with sufficient affinity such that they could be used in affinity chromatograph, supra.

F. Appellant argues that a correlation between the function of binding to FAS-IC and the structure of the protein encoded by DNA sequence having the ability to hybridize to the cDNA encoding SEQ ID NO:2 under moderately stringent conditions is not necessary, in view that it would not be undue experimentation for one to assay to determine which of those bind to FAS-IC.

The arguments are not found to be persuasive.

A correlation between the property of binding to FAS-IC, or the definitive function, such as inducing cytotoxicity or inhibiting FAS-induced cytotoxicity, and the structure of the protein encoded by a DNA sequence having the ability to hybridize to the cDNA encoding SEQ ID

NO:2 under moderately stringent conditions is one of the necessary criteria for a clear written description of the claimed invention, in view that claimed DNA sequence encoding a genus of analog is not defined by a complete or partial structure or other critical physical and/or chemical properties, supra, and that the disclosed DNA sequence encoding SEQ ID NO:2 or its fragment amino acids 153-215, or 130-245 are not representative species, supra. The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by "show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

Concerning Appellant's arguments that said correlation is not necessary, because it would not be undue experimentation for one to assay to determine which of those bind to FAS-IC, Appellant is reminded that "adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of isolating it". The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Thus one would conclude that Appellant did not have possession of the claimed genus of DNA sequences encoding analogs that bind to FAS-IC.

Appellant again argues that the rejection was withdrawn in earlier Office actions, and thus the reinsertion of the rejection by the same Examiner should be given very little weight.

The Examiner apologizes for any inconvenience made. However, the issue remains the same, regardless that the rejection was withdrawn, and then reinstated after review and reconsideration.

Claim Rejections - 35 USC § 112, First Paragraph, Scope

Claims 1-7, 11, 14 remain rejected under 35 USC 112, first paragraph, because while being enabled for a DNA sequence encoding the amino acid sequence of SEQ ID NO:2, or its amino acids 130-245, the specification lacks enablement for a DNA sequence encoding an "analog" of SEQ ID NO:2, which analog binds with the intracellular domain of the FAS ligand receptor (FAS-IC), which DNA sequence is capable of hybridization to the cDNA sequence encoding SEQ ID NO:2 under "moderately stringent conditions", or a DNA coding sequence encoding a fragment of SEQ ID NO:2, which binds FAS-IC.

A. Appellant argues that it is not necessary to know in advance which variants of SEQ ID NO:2 would bind with FAS-IC, and that it is not necessary to decide whether protein chemistry is unpredictable. Appellant argues that analyzing the factors in *In re Wands,* the conclusion must be reached that the experimentation is not undue in the instant application.

The arguments are not found to be persuasive. The Wands analysis has been carefully considered by the Examiner in previous and instant Office actions, and rejection remains. One cannot predict among those analogs that bind to FAS-IC, which mutant or which fragments of SEQ ID NO:2 would bind to FAS-IC with sufficient affinity and having necessary conformation

to have practical use, which use defines and distinguishes the claimed invention from others; e.g., inducing cytotoxicity, or inhibiting FAS-induced cytotoxicity, because of the unpredictability of protein chemistry, as taught by Burgess et al, Lazar et al, Tao et al, and Gillies et al, which applies as well to DNA sequences that encode proteins. In view of such unpredictability and in view of lack of adequate disclosure in the specification, one would conclude that it would be undue experimentation for one of skill in the art to make the claimed DNA sequences encoding analogs, or fragments of SEQ ID NO:2 that bind to FAS-IC, such that said analogs or fragments would bind to FAS-IC with sufficient affinity to have any practical use.

The following Wands analysis is presented by Appellant.

1) The amount of Experimentation.

Appellant argues that the quantity of experimentation may be significant. Appellant argues that mutation however can be randomly made, and is routine in the art, as taught by Sambrook et al. Appellant argues that the amount of experimentation may be permitted to satisfy the enablement requirement, as discussed in *In re Wands,* and that routine screening as in the Wands case does not necessarily amount to undue experimentation.

This is not found to be persuasive.

Although mutation and screening methods are routine in the art, and the amount of experimentation may be permitted to satisfy the enablement requirement in some applications, however, in the instant application, in view of the unpredictability of which mutant or which fragments of SEQ ID NO:2 would bind to FAS-IC with sufficient affinity to have practical use;

e.g., inducing cytotoxicity, or inhibiting FAS-induced cytotoxicity, it would be undue experimentation for one of skill in the art to practice the claimed invention. It is noted that the ability to screen alone does not enable the claimed invention, in view of such unpredictability. Screening assays do not enable the claimed invention because the court found in *Rochester v. Searle*, 358 F.3d 916, Fed Cir, 2004, that screening assays, and by inference suggestions of structural analysis, are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

2) The amount of guidance and direction

Appellant argues that the specification recites Sambrook et al, a laboratory manual used by one of ordinary skill in the art, and that substantial guidance as to a specific binding screen is also provided.

The arguments are not found to be persuasive.

The specification lacks sufficient guidance for one to practice the claimed invention as broadly as claimed. The claimed DNA sequences encode analogs that encompass a genus of sequences of any size, of unknown structure, that bind to FAS-IC with any affinity, which ranges from those having very low affinity to very high affinity, such as peptide mimetics, or agonist or antagonist. The encoded analogs encompass variants of SEQ ID NO:2, or a fragment thereof, having deletion or substitution or addition at any amino acid position of the sequence, provided said analogs bind to FAS-IC. The specification however does not teach where or which deletion or substitution or addition is appropriate such that the encoded analogs would still bind to FAS-IC, or would bind to FAS-IC with sufficient affinity and having necessary conformation to have practical use, e.g., inducing cytotoxicity, or inhibiting FAS-induced cytotoxicity. The

specification does not disclose how to make the claimed DNA sequences encoding analogs, or fragments of SEQ ID NO:2, that would bind to FAS-IC, or bind to FAS-IC with sufficient affinity and having necessary conformation to have any practical use. Disclosure of a method of mutation or binding assay or screening method alone is not sufficient guidance and direction.

3) Working Examples

Appellant argues that binding assay is sufficient as a working example.

The arguments are not found to be persuasive.

Contrary to Appellant's assertion, the specification does not have any working example of the claimed DNA sequences encoding analogs or fragments that bind to FAS-IC, other than the DNA sequence encoding SEQ ID NO:2 and its fragments consisting of amino acids 153-215 or 130-245 of SEQ ID NO:2. Other than SEQ ID NO:2 and its fragments consisting of amino acids 153-215 or 130-245 of SEQ ID NO:2, the specification does not disclose which analogs, or which fragments of SEQ ID NO:2 would bind to FAS-IC, or bind to FAS-IC with sufficient affinity and having necessary conformation to have practical use, e.g., inducing cytotoxicity,or inhibiting FAS-induced cytotoxicity.

Further, binding assay per se is not a working example, because it does not have by itself the sequence structure of a representative number of the claimed analogs, but it requires further experimentation to obtain these sequences. It is noted that screening assays do not enable the claimed invention because the court found in *Rochester v. Searle*, 358 F.3d 916, Fed Cir, 2004, that screening assays, and by inference suggestions of structural analysis, are not sufficient to

enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

4) Nature of the invention.

Appellant argues that the nature of the invention is such that substantial experimentation is acceptable.

The arguments are not found to be persuasive.

The nature of the claimed invention is complex. In view of such complexity, and in view of the above unpredictability, it would be undue experimentation for one of skill in the art to screen for the claimed analogs or fragments.

5) The state of prior art

Appellant argues that moderate stringency hybridization, random mutagenesis and binding assays are all well-documented in the art.

The Examiner takes note that although the method of mutagenesis and binding assays are well known in the art, and although certain specific moderate stringency conditions are described in the art, the claimed moderate stringency hybridization conditions are not defined in the instant specification, and the metes and bounds of which hybridization conditions cannot be determined by one of skill in the art, supra.

6) The unpredictability of the art

Appellant argues that the predictability is not relevant here, and not necessary. Appellant argues that all one need to do is to do the experiment and to screen.

The arguments are not found to be persuasive.

The unpredictability is high for the instant claimed invention, and is an important issue in the instant application. The encoded analogs encompass a genus of sequences of any size of unknown structure, that bind to FAS-IC with any affinity; e.g., a variant of SEQ ID NO:2, or a fragment thereof, having deletion or substitution or addition at any amino acid position of the sequence, provided said sequences bind to FAS-IC. One cannot predict where or which deletion or substitution or addition is appropriate such that the encoded analogs would still bind to FAS-IC, or bind to FAS-IC with sufficient affinity and having necessary conformation to have practical use, such as inducing cytotoxicity, or inhibiting FAS-induced cytotoxicity, view of the unpredictability of protein chemistry as taught by Burgess et al, Lazar et al, Tao et al and Gillies et al, which applies as well to DNA sequences that encode proteins. Similarly, one cannot predict which of the fragments of SEQ ID NO:2, other than amino acids 153-215, or 130-245 of SEQ ID NO:2, bind to FAS-IC, or bind to FAS-IC with sufficient affinity for any practical use. Because of such unpredictability, it would be undue experimentation for one to do the experimentation and to screen for the claimed DNA sequences encoding such analogs or fragments.

B. Appellant argues that the claims do not require that activation of the FAS-IC receptor or any other activity in vivo. Appellant argues that whether the protein can be used to activate the FAS receptor or otherwise have all of the other properties of SEQ ID NO:2 are irrelevant. Appellant argues that the claims only require that the encoded polypeptide binds to FAS-IC. Appellant argues that a claim needs only be supported by a single utility. As a new argument,

Appellant asserts that the encoded protein can be used as an affinity chromatography to isolate FAS-IC or the FAS receptor.

The arguments are not found to be persuasive.

Contrary to Appellant's arguments, whether the protein can activate the FAS receptor (agonist) or otherwise have all of the other properties of SEQ ID NO:2, or as an antagonist is relevant here, because the encoded analogs encompass a broad genus of numerous peptide or protein ligands that bind to FAS-IC, **including** agonist or antagonist, and further because the specification does not disclose the structure of the DNA sequence encoding any such ligands, nor how to make the DNA sequence encoding such ligands, other than the DNA sequence encoding SEQ ID NO:2 or its amino acids 153-215, or 130-245.

In response to Appellant new arguments, to make an affinity column for isolating FAS-IC or FAS-receptor, a binding peptide or protein has to have sufficient binding affinity to FAS-IC or FAS-receptor, and appropriate conformation to fit into FAS receptor. The encoded analogs or fragments of SEQ ID NO:2 that bind to FAS-IC could be of any size and of unknown structure and bind to FAS-IC with **any** binding affinity. One cannot predict which analogs or fragment of SEQ ID NO:2, other than SEQ ID NO:2, or its fragments consisting of amino acids 153-215, or 130-245, that bind to FAS-IC, or bind to FAS-IC with sufficient affinity and having appropriate conformation to confer the property of making affinity chromatography to isolate FAS-IC or the FAS receptor, because not any binding peptide would have sufficient affinity, or binding stability, or necessary conformation to fit into the receptor. Thus, other than SEQ ID NO:2 and its amino acids 153-215, or 130-245, one cannot predict which of the encoded analogs or

fragment of SEQ ID NO:2 could bind to FAS-IC, or bind to FAS-IC with sufficient affinity for making affinity column.

The specification however does not disclose how to make the claimed DNA sequence encoding analogs, or fragments of SEQ ID NO:2 that bind to FAS-IC, other than SEQ ID NO:2, or amino acids 153-215, or 130-245, such that the encoded analogs or fragments would bind to FAS-IC with sufficient affinity suitable for making affinity column to isolate FAS-IC or FAS receptor. It is noted that disclosure of a binding assay, or a mutation method is not sufficient to meet the 112, first paragraph requirement. Screening assays do not enable the claimed invention because the court found in *Rochester v. Searle*, 358 F.3d 916, Fed Cir, 2004, that screening assays, and by inference suggestions of structural analysis, are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

Given the above unpredictability, and in view of the complex nature of the invention, a lack of sufficient disclosure in the specification, and little is known in the art concerning the claimed invention, it would have been undue experimentation for one of skill in the art to practice the claimed invention.

Appellant further argues that the Examiner has not rebutted the Wands analysis made in previous filing of the brief, and repeated herein.

Contrary to Appellant's arguments, all the important issues in the Wands analysis have been carefully considered by the Examiner in previous and instant Office actions.

Appellant argues that the Examiner concedes in the Office action of June 06, 2005 that one could screen for fragments of SEQ ID NO:2 that binds to FAS-IC.

The Examiner takes note that although screening method is known in the art, and

although one could screen for fragments of SEQ ID NO:2 that binds to FAS-IC, i.e., the ability to screen, disclosure of a screening method or the ability to screen is not the same as teaching how to "make" said fragment, and is not adequate to meet the 112, first paragraph requirement, in view of the above unpredictability. It is noted that screening assays do not enable the claimed invention, because the court found in *Rochester v. Searle*, 358 F.3d 916, Fed Cir, 2004, that screening assays, and by inference suggestions of structural analysis, are not sufficient to enable an invention because they are merely a wish or plan for obtaining the claimed chemical invention.

Therefore, because of inadequate disclosure in the specification, and given the above unpredictability, and in view of the complex nature of the invention, and little is known in the art concerning the claimed invention, it would be undue experimentation for one of skill in the art to practice the claimed invention.

Appellant again argues that the rejection was withdrawn in earlier Office actions, and thus the reinsertion of the rejection by the same Examiner should be given very little weight.

The Examiner apologizes for any inconvenience made. However, the issue remains the same, regardless that the rejection was withdrawn, and then reinstated after further review and reconsideration.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

MINH-TAM DAVIS, PhD.

Patent Examiner

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER

Conferees:

Larry Helms, SPE

Gary Nickol, SPE

GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600